EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2349	((546/337) or (514/357)).CCLS.	US-PGPUB; USPAT	OR	OFF	2007/09/17 20:41
L2	1	1 and phosphodiesterase and inhibitor and pyridylacrylamide	US-PGPUB; USPAT	OR	OFF	2007/09/17 20:42
L3	90	1 and phosphodiesterase and inhibitor	US-PGPUB; USPAT	OR	OFF	2007/09/17 20:43
L4	1	(hattori adj tomohisa.inv.)	US-PGPUB	OR	OFF	2007/09/17 20:43
L5	1	(sasaki adj toshinobu.inv.)	US-PGPUB	OR	OFF	2007/09/17 20:43
L6	3	(hasegawa adj yoshihiro.inv.)	US-PGPUB	OR	OFF	2007/09/17 20:44
L7	1	(obata adj tatsuhiro.inv.)	US-PGPUB	OR	OFF	2007/09/17 20:44

10510053

FORMAT

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=> d his

     (FILE 'HOME' ENTERED AT 18:41:21 ON 17 SEP 2007)

     FILE 'REGISTRY' ENTERED AT 18:41:31 ON 17 SEP 2007

     FILE 'HCAPLUS' ENTERED AT 18:41:33 ON 17 SEP 2007
L1           465 S PHOSPHODIESTERASE () IV () INHIBITOR?
L2            10 S L1 AND BRONCHIAL () ASTHMA?
L3             1 S L2 AND REVIEW/DT

=> s l1 and chronic () bronchitis?
         223536 CHRONIC
              7 CHRONICS
         223540 CHRONIC
                   (CHRONIC OR CHRONICS)
           6773 BRONCHITIS?
           2928 CHRONIC (W) BRONCHITIS?
L4           25 L1 AND CHRONIC (W) BRONCHITIS?

=> s l4 and review/dt
        2068307 REVIEW/DT
L5            0 L4 AND REVIEW/DT

=> s l1 and atopic () dermatitis?
          10448 ATOPIC
            161 ATOPICS
          10488 ATOPIC
                   (ATOPIC OR ATOPICS)
          19370 DERMATITIS?
           4529 ATOPIC (W) DERMATITIS?
L6           11 L1 AND ATOPIC (W) DERMATITIS?

=> s l6 and review/dt
        2068307 REVIEW/DT
L7            2 L6 AND REVIEW/DT

=> s l7 not l3
L8            2 L7 NOT L3

=> d l8, ibib abs hitstr, 1-2

L8   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         1999:523083  HCAPLUS
DOCUMENT NUMBER:          131:266413
TITLE:                    Phosphodiesterase 4 inhibitors as novel
                          anti-inflammatory agents
AUTHOR(S):                Doherty, Annette M.
CORPORATE SOURCE:         Institut de Recherche Jouveinal/Parke-Davis, Fresnes,
                          94265, Fr.
SOURCE:                   Current Opinion in Chemical Biology (1999), 3(4),
                          466-473
                          CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER:                Current Biology Publications
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
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Updated Search

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	BEILSTEIN updated with new compounds
NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 15	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16	AUG 27	USPATOLD now available on STN
NEWS 17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB: New SDI frequency MONTHLY available now
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents

NEWS EXPRESS 05 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 05 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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AB A review with 83 refs. Preclin. and clin. studies of phosphodiesterase 4 inhibitors have shown that these agents may find utility in a wide range of inflammatory disorders, including asthma, chronic obstructive pulmonary disease, atopic dermatitis, rheumatoid arthritis, multiple sclerosis and various neurol. disorders. The future of this class of drugs will depend upon the ability to demonstrate a reasonable safety margin against emesis and other typical phosphodieserase (PDE4) side effects, as well as in identification of the inflammatory disorder(s) most relevant to PDE4 inhibition.
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:568524 HCAPLUS
DOCUMENT NUMBER: 125:237241
TITLE: New therapeutic approaches to atopic dermatitis
AUTHOR(S): Bird, John; Montana, John
CORPORATE SOURCE: Chiroscience Ltd., Cambridge, CB4 4WE, UK
SOURCE: Expert Opinion on Investigational Drugs (1996), 5(9), 1173-1180
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 49 refs. Atopic dermatitis (AD) is a chronic inflammatory skin disease which affects some 10-15% of the population during childhood. The prevalence of the disease is increasing and there are few, if any, current therapies which are directed at the underlying cause of the disease. A better understanding of the mechanisms of AD is starting to offer potential therapeutic approaches to this disease. The understanding of the role of cytokines in AD, in particular interleukin-4, interferon-gamma and tumor necrosis factor-alpha, has indicated several potential approaches, including inhibition of cytokine processing (matrix metalloproteinase inhibitors), inhibition of cytokine release (phosphodiesterase type IV inhibitors) and modulation of cytokine levels, as well as newer approaches to immunomodulation.

=> d his

(FILE 'HOME' ENTERED AT 18:41:21 ON 17 SEP 2007)

FILE 'REGISTRY' ENTERED AT 18:41:31 ON 17 SEP 2007

FILE 'HCAPLUS' ENTERED AT 18:41:33 ON 17 SEP 2007
L1 465 S PHOSPHODIESTERASE () IV () INHIBITOR?
L2 10 S L1 AND BRONCHIAL () ASTHMA?
L3 1 S L2 AND REVIEW/DT
L4 25 S L1 AND CHRONIC () BRONCHITIS?
L5 0 S L4 AND REVIEW/DT
L6 11 S L1 AND ATOPIC () DERMATITIS?
L7 2 S L6 AND REVIEW/DT
L8 2 S L7 NOT L3

=> s l1 and hives?
333 HIVES?
L9 0 L1 AND HIVES?

Updated Search

10510053

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FILE 'HOME' ENTERED AT 18:41:21 ON 17 SEP 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 SEP 2007 HIGHEST RN 947312-67-6
DICTIONARY FILE UPDATES: 16 SEP 2007 HIGHEST RN 947312-67-6

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	0.66

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FILE LAST UPDATED: 16 Sep 2007 (20070916/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s phosphodiesterase () iv () inhibitor?
         27289 PHOSPHODIESTERASE
          2911 PHOSPHODIESTERASES
         27881 PHOSPHODIESTERASE
                 (PHOSPHODIESTERASE OR PHOSPHODIESTERASES)
        532034 IV
          1017 IVS
        532949 IV
                 (IV OR IVS)
       1059180 INHIBITOR?
L1         465 PHOSPHODIESTERASE (W) IV (W) INHIBITOR?

=> s l1 and bronchial () asthma?
         18230 BRONCHIAL
             4 BRONCHIALS
         18234 BRONCHIAL
                 (BRONCHIAL OR BRONCHIALS)
         38000 ASTHMA?
          4721 BRONCHIAL (W) ASTHMA?
L2          10 L1 AND BRONCHIAL (W) ASTHMA?

=> s l2 and review/dt
       2068307 REVIEW/DT
L3            1 L2 AND REVIEW/DT

=> d l3, ibib abs hitstr, 1

L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         1999:732844  HCAPLUS
DOCUMENT NUMBER:          132:202457
TITLE:                    Ariflo SmithKline Beecham
AUTHOR(S):                Brown, William
CORPORATE SOURCE:         Somerville, NJ, 08876-8139, USA
SOURCE:                   Current Opinion in Cardiovascular, Pulmonary & Renal
                          Investigational Drugs (1999), 1(4), 506-515
                          CODEN: CCPRFX; ISSN: 1464-8482
PUBLISHER:                Current Drugs Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review with .apprx.120 refs.  Ariflo (SB-207499) is a phosphodiesterase
     (PDE)4 inhibitor under development by SmithKline Beecham and in phase III
     and II clin. trials as a potential treatment for chronic obstructive
     pulmonary disease (COPD) and asthma, resp.  It has commenced phase II
     trials as a treatment for bronchial asthma in Japan.
     In Feb. 1999, Merrill Lynch predicted that Ariflo would be launched by the
     end of 2000 or early 2001 with first year sales of UK £25 million
     rising to UK £175 million in 2003.  In July 1999, Merrill Lynch
     forecast filing of Ariflo by the second half of 2000.  In Feb. 1999, ABN
     Amro predicted sales of UK £52 million in 2001, rising to UK £254
     million in 2005.
REFERENCE COUNT:          157   THERE ARE 157 CITED REFERENCES AVAILABLE FOR
                                THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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Updated Search

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```
=> s l1 and allergic () rhinitis?
         37453 ALLERGIC
            78 ALLERGICS
         37476 ALLERGIC
                  (ALLERGIC OR ALLERGICS)
          7251 RHINITIS?
          4716 ALLERGIC (W) RHINITIS?
L10         32 L1 AND ALLERGIC (W) RHINITIS?

=> s l10 and review/dt
       2068307 REVIEW/DT
L11          0 L10 AND REVIEW/DT

=> s l1 and conjunctivitis?
          3086 CONJUNCTIVITIS?
L12         24 L1 AND CONJUNCTIVITIS?

=> s l12 and review/dt
       2068307 REVIEW/DT
L13          0 L12 AND REVIEW/DT

=> s l1 and rheumatoid () arthritis?
         34295 RHEUMATOID
            11 RHEUMATOIDS
         34299 RHEUMATOID
                  (RHEUMATOID OR RHEUMATOIDS)
         48451 ARTHRITIS?
         30534 RHEUMATOID (W) ARTHRITIS?
L14         45 L1 AND RHEUMATOID (W) ARTHRITIS?

=> s l14 and review/dt
       2068307 REVIEW/DT
L15          3 L14 AND REVIEW/DT

=> d l15, ibib abs hitstr, 1-3

L15  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2005:603862  HCAPLUS
DOCUMENT NUMBER:         143:259162
TITLE:                   Inhibitors of PDE4: a review of recent patent
                         literature
AUTHOR(S):               Odingo, Joshua O.
CORPORATE SOURCE:        Department of Medicinal Chemistry, Division of
                         Chemical Sciences, ICOS Corporation, Bothell, WA,
                         98021, USA
SOURCE:                  Expert Opinion on Therapeutic Patents (2005), 15(7),
                         773-787
                         CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER:               Ashley Publications Ltd.
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
AB   A review.  The preregistration of roflumilast and the preapproval by the
     US Food and Drug Administration of cilomilast highlight the continued,
     albeit slow, progress towards a selective PDE4 inhibitor for the treatment
     of inflammatory diseases, such as asthma and chronic obstructive pulmonary
     disease.  Whereas the potential therapeutic utility of PDE4 inhibition has
     been demonstrated in various preclin. animal models (e.g., in
     rheumatoid arthritis and multiple sclerosis), clin.
     evaluation has been restricted by dose-limiting side effects, mainly
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nausea and emesis. Continued disclosure of novel, selective and chemical diverse inhibitors by pharmaceutical companies demonstrates the great interest in PDE4 research. This review focuses on the PDE4 patent literature regarding clin. developments since 2002, and discusses disclosed PDE4 inhibitors from a medicinal chemical perspective.
REFERENCE COUNT: 142 THERE ARE 142 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:523083 HCAPLUS
DOCUMENT NUMBER: 131:266413
TITLE: Phosphodiesterase 4 inhibitors as novel anti-inflammatory agents
AUTHOR(S): Doherty, Annette M.
CORPORATE SOURCE: Institut de Recherche Jouveinal/Parke-Davis, Fresnes, 94265, Fr.
SOURCE: Current Opinion in Chemical Biology (1999), 3(4), 466-473
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 83 refs. Preclin. and clin. studies of phosphodiesterase 4 inhibitors have shown that these agents may find utility in a wide range of inflammatory disorders, including asthma, chronic obstructive pulmonary disease, atopic dermatitis, rheumatoid arthritis, multiple sclerosis and various neurol. disorders. The future of this class of drugs will depend upon the ability to demonstrate a reasonable safety margin against emesis and other typical phosphodieserase (PDE4) side effects, as well as in identification of the inflammatory disorder(s) most relevant to PDE4 inhibition.
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:125736 HCAPLUS
DOCUMENT NUMBER: 130:332099
TITLE: Potential of phosphodiesterase type IV inhibitors in the treatment of rheumatoid arthritis
AUTHOR(S): Souness, John E.; Foster, Martyn
CORPORATE SOURCE: Department of Cell Biology, Discovery Biology, Essex, RM10 7XS, UK
SOURCE: IDrugs (1998), 1(5), 541-553
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 95 refs. Rheumatoid arthritis (RA) is a crippling autoimmune disease which afflicts over 1% of the population. Non-steroidal anti-inflammatory drugs are widely used palliatives, but these disease-modifying drugs are of variable and limited efficacy, and are frequently associated with side-effects which restrict their use. Agents that elevate cAMP, including cAMP-specific phosphodiesterase (PDE) inhibitors, possess a profile of anti-inflammatory activities which suggest potential benefit in RA. In several rodent RA models, PDE IV inhibitors reduce the incidence and severity of disease symptoms and histol. anal. reveals a significant, beneficial effect on joint pathol.

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Several potential mechanisms may underpin the anti-arthritic actions of PDE IV inhibitors. These include inhibition of tumor necrosis factor (TNF)-α release, increase of interleukin (IL)-10 release, and suppression of T-lymphocyte function, as well as direct, protective effects on cartilage and bone. Although stimulation of the hypothalamic-pituitary-adrenal axis in rodents has previously been suggested as a possible mechanism by which PDE IV inhibitors exert their anti-arthritic effects, recent data question its importance. For example, RP-73401 ameliorates disease severity in Streptococcal cell wall-induced arthritis in Lewis rats, a strain whose susceptibility to this disease has been attributed to a defective HPA response, without affecting either ACTH or corticosterone levels. In a small clin. study, RA patients treated with low doses of RP-73401, showed a pos. (non-significant) trend in respect of serum concns. of IL-6 and CRP. Although levels of TNFα and IL-1β were unaffected, patients reported some symptomatic relief. The administration of higher doses was prohibited due to side-effects and compds. with an improved therapeutic window will have to be identified to further explore the potential of PDE IV inhibitors in the treatment of RA.

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 18:41:21 ON 17 SEP 2007)

FILE 'REGISTRY' ENTERED AT 18:41:31 ON 17 SEP 2007

FILE 'HCAPLUS' ENTERED AT 18:41:33 ON 17 SEP 2007

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L1          465 S PHOSPHODIESTERASE () IV () INHIBITOR?
L2           10 S L1 AND BRONCHIAL () ASTHMA?
L3            1 S L2 AND REVIEW/DT
L4           25 S L1 AND CHRONIC () BRONCHITIS?
L5            0 S L4 AND REVIEW/DT
L6           11 S L1 AND ATOPIC () DERMATITIS?
L7            2 S L6 AND REVIEW/DT
L8            2 S L7 NOT L3
L9            0 S L1 AND HIVES?
L10          32 S L1 AND ALLERGIC () RHINITIS?
L11           0 S L10 AND REVIEW/DT
L12          24 S L1 AND CONJUNCTIVITIS?
L13           0 S L12 AND REVIEW/DT
L14          45 S L1 AND RHEUMATOID () ARTHRITIS?
L15           3 S L14 AND REVIEW/DT

=> s l1 and gonarthrosis
            45 GONARTHROSIS
L16          1 L1 AND GONARTHROSIS

=> s l16 and review/dt
       2068307 REVIEW/DT
L17           0 L16 AND REVIEW/DT

=> s l1 and septicemia?
          6014 SEPTICEMIA?
L18           7 L1 AND SEPTICEMIA?

=> s l18 and review/dt
       2068307 REVIEW/DT
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Updated Search

10510053

```
L19          0 L18 AND REVIEW/DT

=> s l1 and ulcerative () colitis?
          8739 ULCERATIVE
             2 ULCERATIVES
          8741 ULCERATIVE
                 (ULCERATIVE OR ULCERATIVES)
         12435 COLITIS?
          7879 ULCERATIVE (W) COLITIS?
L20         39 L1 AND ULCERATIVE (W) COLITIS?

=> s l20 and review/dt
       2068307 REVIEW/DT
L21          0 L20 AND REVIEW/DT

=> s l1 and manic-depressive () psychosis?
          2556 MANIC
            23 MANICS
          2565 MANIC
                 (MANIC OR MANICS)
          8994 DEPRESSIVE
           324 DEPRESSIVES
          9191 DEPRESSIVE
                 (DEPRESSIVE OR DEPRESSIVES)
           889 MANIC-DEPRESSIVE
                 (MANIC(W)DEPRESSIVE)
          6322 PSYCHOSIS?
           195 MANIC-DEPRESSIVE (W) PSYCHOSIS?
L22          0 L1 AND MANIC-DEPRESSIVE (W) PSYCHOSIS?

=> s l1 and schizophrenia?
         17744 SCHIZOPHRENIA?
L23         12 L1 AND SCHIZOPHRENIA?

=> s l23 and review/dt
       2068307 REVIEW/DT
L24          0 L23 AND REVIEW/DT

=> s l1 and crohn's () disease?
MISMATCHED QUOTE 'CROHN'S'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> s l1 and chrohn?
            12 CHROHN?
L25          0 L1 AND CHROHN?

=> d his

     (FILE 'HOME' ENTERED AT 18:41:21 ON 17 SEP 2007)

     FILE 'REGISTRY' ENTERED AT 18:41:31 ON 17 SEP 2007

     FILE 'HCAPLUS' ENTERED AT 18:41:33 ON 17 SEP 2007
L1          465 S PHOSPHODIESTERASE () IV () INHIBITOR?
L2           10 S L1 AND BRONCHIAL () ASTHMA?
L3            1 S L2 AND REVIEW/DT
L4           25 S L1 AND CHRONIC () BRONCHITIS?
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Updated Search

10510053

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L5            0 S L4 AND REVIEW/DT
L6           11 S L1 AND ATOPIC () DERMATITIS?
L7            2 S L6 AND REVIEW/DT
L8            2 S L7 NOT L3
L9            0 S L1 AND HIVES?
L10          32 S L1 AND ALLERGIC () RHINITIS?
L11           0 S L10 AND REVIEW/DT
L12          24 S L1 AND CONJUNCTIVITIS?
L13           0 S L12 AND REVIEW/DT
L14          45 S L1 AND RHEUMATOID () ARTHRITIS?
L15           3 S L14 AND REVIEW/DT
L16           1 S L1 AND GONARTHROSIS
L17           0 S L16 AND REVIEW/DT
L18           7 S L1 AND SEPTICEMIA?
L19           0 S L18 AND REVIEW/DT
L20          39 S L1 AND ULCERATIVE () COLITIS?
L21           0 S L20 AND REVIEW/DT
L22           0 S L1 AND MANIC-DEPRESSIVE () PSYCHOSIS?
L23          12 S L1 AND SCHIZOPHRENIA?
L24           0 S L23 AND REVIEW/DT
L25           0 S L1 AND CHROHN?

=> s l1 and review/dt
       2068307 REVIEW/DT
L26          25 L1 AND REVIEW/DT

=> s l26 and pd < may 2003
      23692794 PD < MAY 2003
                 (PD<20030500)
L27          22 L26 AND PD < MAY 2003

=> d l27, ibib abs hitstr, 1-22

L27  ANSWER 1 OF 22  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2002:310782  HCAPLUS
DOCUMENT NUMBER:          137:15147
TITLE:                    The antidepressant and antiinflammatory effects of
                          rolipram in the central nervous system
AUTHOR(S):                Zhu, Jie; Mix, Eilhard; Winblad, Bengt
CORPORATE SOURCE:         Division of Geriatric Medicine, Huddinge University
                          Hospital, Stockholm, S-141 86, Swed.
SOURCE:                   CNS Drug Reviews (2001), 7(4), 387-398
                          CODEN: CDREFB; ISSN: 1080-563X
PUBLISHER:                Neva Press
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB    A review.  Rolipram is a selective inhibitor of phosphodiesterases (PDE)
      IV, especially of the subtype PDE IVB.  These phosphodiesterases are
responsible
      for hydrolysis of the cyclic nucleotides cAMP and cGMP, particularly in
      nerve and immune cells.  Consequences of rolipram-induced elevation of
      intracellular cAMP are increased synthesis and release of norepinephrine,
      which enhance central noradrenergic transmission, and suppress expression
      of proinflammatory cytokines and other mediators of inflammation.  In
      humans and animals rolipram produces thereby a variety of biol. effects.
      These effects include attenuation of endogenous depression and
      inflammation in the central nervous system (CNS), both effects are of
      potential clin. relevance.  There are some discrepancies between in vitro
      and in vivo effects of rolipram, as well as between results obtained in
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Updated Search

animal models and clin. studies. The clin. use of rolipram is limited because of its behavioral and other side effects. Newly developed selective PDE IV inhibitors with presumably higher potency and lower toxicity are currently under investigation.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:562815 HCAPLUS
DOCUMENT NUMBER: 136:63429
TITLE: Phosphodiesterase inhibitors
AUTHOR(S): Cooper, Nicky; Krishna, Mamidipudi Thirumala; Gristwood, Robert; Holgate, Stephen
CORPORATE SOURCE: Biology Celltech Chiroscience, Cambridge, UK
SOURCE: Therapeutic Immunology (2nd Edition) (2001), 140-149. Editor(s): Austen, K. Frank. Blackwell Science, Inc.: Malden, Mass.
CODEN: 69BPIR
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review focuses on theophylline and inhibitors of type IV phosphodiesterase (PDE) and their roles in the treatment of asthma. The identification of many ways that cyclic nucleotide PDEs vary in their expression in different cells and tissues provides strong evidence that specific inhibitors could be developed in relation to different diseases.
REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:64754 HCAPLUS
DOCUMENT NUMBER: 133:4
TITLE: Potential of PDE4 inhibitors in the treatment of osteopenia
AUTHOR(S): Kasugai, Shohei; Miyamoto, Ken-Ichi
CORPORATE SOURCE: Dept. of Pharmacology, Faculty of Dentistry, Tokyo Medical and Dental University, Tokyo, 113-8549, Japan
SOURCE: Drug News & Perspectives (1999), 12(9), 529-534
CODEN: DNPEED; ISSN: 0214-0934
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 41 refs. Osteoporosis is characterized by the loss of bone that can lead to fractures in sites such as the hip and spine. The number of patients with this disease is increasing in developed countries because of the increase in the aged population. Although several drugs are currently used to treat osteoporosis, the development of effective drugs for this condition is still greatly desired. The authors are interested in prostaglandin E2 (PGE2) and parathyroid hormone (PTH) because systemic administration with these mols. increases bone mass in exptl. animals and also in humans. The authors established a rat bone marrow culture system in which bone-like tissue is formed, reproduced the anabolic effect of PGE2 and PTH in this culture system, and observed that this anabolic effect is mainly mediated by an increase in the cAMP level. Since phosphodiesterase 4 (PDE4) is an enzyme that specifically degrades cAMP, PDE4 inhibitors could mimic the effects of PGE2 and PTH. Indeed, PDE4 inhibitors increased bone-like tissue formation in the culture system and increased bone mass when administered to rats and mice. Furthermore, PDE4 inhibitors exerted therapeutic effects in rat osteopenia models

(tumor-bearing rat, neurectomized rats, and ovariectomized female rats). These results indicate that PDE4 inhibitors could be candidates for therapeutic drugs for osteopenia, including osteoporosis.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:732845 HCAPLUS
DOCUMENT NUMBER: 132:202458
TITLE: Arofylline Almirall-Prodesfarma
AUTHOR(S): Norman, Peter
CORPORATE SOURCE: Norman Consulting, Burnham Buckinghamshire, SL1 8JW, UK
SOURCE: Current Opinion in Cardiovascular, Pulmonary & Renal Investigational Drugs (1999), 1(4), 516-518
CODEN: CCPRFX; ISSN: 1464-8482
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 21 refs. Arofylline (LAS-31025) is a PDE4 inhibitor under development by Almirall-Prodesfarma as a potential treatment for asthma. An oral formulation is in phase III clin. trials, while an inhaled formulation has entered phase I clin. trials.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:732844 HCAPLUS
DOCUMENT NUMBER: 132:202457
TITLE: Ariflo SmithKline Beecham
AUTHOR(S): Brown, William
CORPORATE SOURCE: Somerville, NJ, 08876-8139, USA
SOURCE: Current Opinion in Cardiovascular, Pulmonary & Renal Investigational Drugs (1999), 1(4), 506-515
CODEN: CCPRFX; ISSN: 1464-8482
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.120 refs. Ariflo (SB-207499) is a phosphodiesterase (PDE)4 inhibitor under development by SmithKline Beecham and in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. It has commenced phase II trials as a treatment for bronchial asthma in Japan. In Feb. 1999, Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of UK £25 million rising to UK £175 million in 2003. In July 1999, Merrill Lynch forecast filing of Ariflo by the second half of 2000. In Feb. 1999, ABN Amro predicted sales of UK £52 million in 2001, rising to UK £254 million in 2005.
REFERENCE COUNT: 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:581087 HCAPLUS
DOCUMENT NUMBER: 131:266429
TITLE: The therapeutic potential of PDE4 inhibitors
AUTHOR(S): Dyke, Hazel J.; Montana, John G.
CORPORATE SOURCE: Celltech Chiroscience, Cambridge Science Park, Cambridge, CB4 4WE, UK

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SOURCE: Expert Opinion on Investigational Drugs (1999), 8(9), 1301-1325
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 284 refs. Phosphodiesterase enzymes are responsible for the inactivation of cAMP and cGMP. Phosphodiesterase 4 (PDE4) is a cAMP specific phosphodiesterase expressed in inflammatory cells such as eosinophils. Inhibition of PDE4 results in an elevation of cAMP in these cells, which in turn downregulates the inflammatory response. The anti-inflammatory effects of PDE4 inhibitors have been well documented both in vitro and in vivo in a variety of animal models. The potential use of PDE4 inhibitors as anti-inflammatory agents for the treatment of asthma and other inflammatory disorders has received considerable attention from the pharmaceutical industry, but to date, there are no selective PDE4 inhibitors on the market. Early PDE4 inhibitors, typified by rolipram, suffered from dose-limiting side effects, including nausea and emesis, which severely restricted their therapeutic utility. Second generation compds., including CDP840 and SB207499 (Ariflo), have been identified with reduced side effect liability. Recent evidence suggests a correlation between side effects and the ability of compds. to bind at the so-called high affinity rolipram binding site (HPDE), while beneficial effects appear to correlate with binding at the catalytic site. A number of companies are actively pursuing compds. which exhibit improved affinity for the catalytic site and reduced affinity for the HPDE, in the expectation that this will provide compds. with an improved therapeutic index.

REFERENCE COUNT: 285 THERE ARE 285 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:523083 HCAPLUS
DOCUMENT NUMBER: 131:266413
TITLE: Phosphodiesterase 4 inhibitors as novel anti-inflammatory agents
AUTHOR(S): Doherty, Annette M.
CORPORATE SOURCE: Institut de Recherche Jouveinal/Parke-Davis, Fresnes, 94265, Fr.
SOURCE: Current Opinion in Chemical Biology (1999), 3(4), 466-473
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 83 refs. Preclin. and clin. studies of phosphodiesterase 4 inhibitors have shown that these agents may find utility in a wide range of inflammatory disorders, including asthma, chronic obstructive pulmonary disease, atopic dermatitis, rheumatoid arthritis, multiple sclerosis and various neurol. disorders. The future of this class of drugs will depend upon the ability to demonstrate a reasonable safety margin against emesis and other typical phosphodieserase (PDE4) side effects, as well as in identification of the inflammatory disorder(s) most relevant to PDE4 inhibition.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN

Updated Search

10510053

ACCESSION NUMBER: 1999:125736 HCAPLUS
DOCUMENT NUMBER: 130:332099
TITLE: Potential of phosphodiesterase type IV inhibitors in the treatment of rheumatoid arthritis
AUTHOR(S): Souness, John E.; Foster, Martyn
CORPORATE SOURCE: Department of Cell Biology, Discovery Biology, Essex, RM10 7XS, UK
SOURCE: IDrugs (1998), 1(5), 541-553
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 95 refs. Rheumatoid arthritis (RA) is a crippling autoimmune disease which afflicts over 1% of the population. Non-steroidal anti-inflammatory drugs are widely used palliatives, but these disease-modifying drugs are of variable and limited efficacy, and are frequently associated with side-effects which restrict their use. Agents that elevate cAMP, including cAMP-specific phosphodiesterase (PDE) inhibitors, possess a profile of anti-inflammatory activities which suggest potential benefit in RA. In several rodent RA models, PDE IV inhibitors reduce the incidence and severity of disease symptoms and histol. anal. reveals a significant, beneficial effect on joint pathol. Several potential mechanisms may underpin the anti-arthritic actions of PDE IV inhibitors. These include inhibition of tumor necrosis factor (TNF)-α release, increase of interleukin (IL)-10 release, and suppression of T-lymphocyte function, as well as direct, protective effects on cartilage and bone. Although stimulation of the hypothalamic-pituitary-adrenal axis in rodents has previously been suggested as a possible mechanism by which PDE IV inhibitors exert their anti-arthritic effects, recent data question its importance. For example, RP-73401 ameliorates disease severity in Streptococcal cell wall-induced arthritis in Lewis rats, a strain whose susceptibility to this disease has been attributed to a defective HPA response, without affecting either ACTH or corticosterone levels. In a small clin. study, RA patients treated with low doses of RP-73401, showed a pos. (non-significant) trend in respect of serum concns. of IL-6 and CRP. Although levels of TNFα and IL-1β were unaffected, patients reported some symptomatic relief. The administration of higher doses was prohibited due to side-effects and compds. with an improved therapeutic window will have to be identified to further explore the potential of PDE IV inhibitors in the treatment of RA.
REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:98886 HCAPLUS
DOCUMENT NUMBER: 130:246098
TITLE: Drug treatment of asthma in the 1990s; Achievements and new strategies
AUTHOR(S): Tavakkoli, Aryan; Rees, P. John
CORPORATE SOURCE: Respiratory Medicine, Guy's Hospital, London, UK
SOURCE: Drugs (1999), 57(1), 1-8
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 59 refs. Asthma is an inflammatory condition of the airways. First-line therapy involves the use of inhaled corticosteroids as anti-inflammatory agents to control the underlying process. Bronchodilators are used for symptom relief. Short-acting β-agonists

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provide rapid relief of bronchoconstriction, whereas long-acting β-agonists control the symptoms and reduce the frequency of exacerbations when combined with inhaled corticosteroids. Anticholinergic bronchodilators have a minor role in acute exacerbations and in patients troubled by adverse effects from β-agonists. Theophylline has a bronchodilator action in asthma, but its role as an anti-inflammatory agent needs to be examined further. Because of their toxicity, corticosteroid-sparing agents have a limited role, being restricted to patients with severe uncontrolled asthma. New selective phosphodiesterase IV inhibitors show both anti-inflammatory and bronchodilator characteristics with fewer adverse effects. Other new approaches to the control of inflammation come from the antileukotriene drugs, which improve pulmonary function in patients with chronic asthma. The antileukotrienes have shown promising results, especially in the treatment of asthma caused by aspirin (acetylsalicylic acid), exercise and cold air. Other new therapies being studied include anti-IgE, antitryptase and anti-CD4 agents. These newer possibilities suggest that the range of available treatment options will expand significantly over the next decade.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:803291 HCAPLUS
DOCUMENT NUMBER: 130:148137
TITLE: Phosphodiesterases 4 inhibitors
AUTHOR(S): Burnouf, Catherine; Pruniaux, Marie-Pierre; Szilagyi, Corinne M.
CORPORATE SOURCE: Institut de Recherche Jouveinal/Parke-Davis, Fresnes, 94265, Fr.
SOURCE: Annual Reports in Medicinal Chemistry (1998), 33, 91-109
CODEN: ARMCBI; ISSN: 0065-7743
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 125 refs. of antiasthmatic and anti-inflammatory PDE4 inhibitors which are presently in clin. development. (c) 1998 Academic Press.
REFERENCE COUNT: 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:616407 HCAPLUS
DOCUMENT NUMBER: 130:79
TITLE: SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor
AUTHOR(S): Silvestre, J.; Graul, A.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (1998), 23(6), 607-615
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A brief review with 49 refs. is given on cis-4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]cyclohexane-1-carboxylic acid, SB-207499, ariflo, selected for treating allergic and inflammatory diseases. The 2nd-generation

phosphodiesterase (PDE) 4 inhibitor SB-207499 under development is compared with corresponding drugs like rolipram, atizoram, piclamilast, V-11294A, and T-440. The PDE 4 inhibitory activities, the high-affinity rolipram binding site, the in vitro inhibitory activities on tumor necrosis factor-α production, on bronchoconstriction, and on cloned human PDE 4 subtypes are compared. Pharmacol. actions, pharmacokinetics, pharmacodynamics, and clin. studies are described. SB-207499 is currently in phase II testing in adults and pediatric patients with asthma and in phase III trials in patients with chronic obstructive pulmonary disease.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:610917 HCAPLUS
DOCUMENT NUMBER: 127:272040
TITLE: T-440. Antiasthmatic phosphodiesterase IV inhibitor
AUTHOR(S): Graul, A.; Leeson, P.; Castaner, J.
CORPORATE SOURCE: Prous Sci. Publishers, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (1997), 22(7), 729-732
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 13 refs. on the synthesis, pharmacol. action and metabolism of T-440.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:455304 HCAPLUS
DOCUMENT NUMBER: 127:134341
TITLE: The rabbit as an animal model of allergy, asthma and airway hyperresponsiveness
AUTHOR(S): Herd, C. M.; Page, C. P.
CORPORATE SOURCE: Biomedical Sciences Division, Pharmacology Group, King's College, University of London, London, SW3 6LX, UK
SOURCE: Allergy and Allergic Diseases (1997), Volume 2, 1079-1092. Editor(s): Kay, A. B. Blackwell: Oxford, UK.
CODEN: 64SCAU
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 133 refs. discussing neonatal immunization, latex-induced hypersensitivity, allergic cutaneous responses, pulmonary function methodol., airway hyperresponsiveness, antigen-induced airway responses in vivo, inflammatory mediators, the effects of drugs on antigen-induced airway responses, airway hyperresponsiveness and airway wall remodeling, airway smooth muscle, IgE anaphylaxis, and sinusitis.

L27 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:365283 HCAPLUS
DOCUMENT NUMBER: 127:75336
TITLE: Phosphodiesterase inhibitors: knockout drops?
AUTHOR(S): Raeburn, David; Karlsson, Jan-Anders
CORPORATE SOURCE: Rhone-Poulenc Rorer Ltd, Dagenham Research Centre, Dagenham, RM10 7XS, UK
SOURCE: Journal of Pharmacy and Pharmacology (1997),

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49(Suppl. 3), 19-24
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Royal Pharmaceutical Society of Great Britain
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 30 refs., on the use of phosphodiesterase inhibitors with combined bronchodilator and antiinflammatory profile in asthma therapy.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:738898 HCAPLUS
DOCUMENT NUMBER: 126:14217
TITLE: Chronic pulmonary inflammation and other therapeutic applications of PDE IV inhibitors
AUTHOR(S): Stafford, Jeffrey A.; Feldman, Paul L.
CORPORATE SOURCE: Glaxo Wellcome Research, Research Triangle Park, NC, 27709, USA
SOURCE: Annual Reports in Medicinal Chemistry (1996), 31, 71-80
CODEN: ARMCBI; ISSN: 0065-7743
PUBLISHER: Academic
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 74 refs. of anti-inflammatory effects of adenosine cyclic 3',5'-phosphate phosphodiesterase inhibitors.

L27 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:714621 HCAPLUS
DOCUMENT NUMBER: 126:171
TITLE: Enzymic and functional aspects of dual-selective PDE3/4 inhibitors
AUTHOR(S): Hatzelmann, Armin; Engelstaetter, Renate; Morley, John; Mazzoni, Lazzarro
CORPORATE SOURCE: Department Biochemistry, Byk Gulden Pharmaceuticals, Konstanz, D-78403, Germany
SOURCE: Phosphodiesterase Inhibitors (1996), 147-160. Editor(s): Schudt, Christian; Dent, Gordon; Rabe, Klaus F. Academic: London, UK.
CODEN: 63RBAF
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with over 60 refs.

L27 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:714618 HCAPLUS
DOCUMENT NUMBER: 126:168
TITLE: Interaction of PDE4 inhibitors with enzymes and cell functions
AUTHOR(S): Dent, Gordon; Giembycz, Mark A.
CORPORATE SOURCE: Krankenhaus Grosshansdorf, Zentrum fur Pneumologie und Thoraxchirurgie, Grosshansdorf, D-22927, Germany
SOURCE: Phosphodiesterase Inhibitors (1996), 111-126. Editor(s): Schudt, Christian; Dent, Gordon; Rabe, Klaus F. Academic: London, UK.
CODEN: 63RBAF
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB Review with over 120 refs.

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L27 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:703179 HCAPLUS
DOCUMENT NUMBER: 126:77
TITLE: Phosphodiesterase IV inhibitors as potential therapeutic agents in allergic disease
AUTHOR(S): Giembycz, Mark A.; Souness, John E.
CORPORATE SOURCE: Royal Brompton National Heart and Lung Institute, London, UK
SOURCE: Clinical Allergy and Immunology (1996), 8(Immunopharmacology of Allergic Diseases), 523-559
CODEN: CALMEH; ISSN: 1075-7910
PUBLISHER: Dekker
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 238 refs.

L27 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:568524 HCAPLUS
DOCUMENT NUMBER: 125:237241
TITLE: New therapeutic approaches to atopic dermatitis
AUTHOR(S): Bird, John; Montana, John
CORPORATE SOURCE: Chiroscience Ltd., Cambridge, CB4 4WE, UK
SOURCE: Expert Opinion on Investigational Drugs (1996), 5(9), 1173-1180
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 49 refs. Atopic dermatitis (AD) is a chronic inflammatory skin disease which affects some 10-15% of the population during childhood. The prevalence of the disease is increasing and there are few, if any, current therapies which are directed at the underlying cause of the disease. A better understanding of the mechanisms of AD is starting to offer potential therapeutic approaches to this disease. The understanding of the role of cytokines in AD, in particular interleukin-4, interferon-gamma and tumor necrosis factor-alpha, has indicated several potential approaches, including inhibition of cytokine processing (matrix metalloproteinase inhibitors), inhibition of cytokine release (phosphodiesterase type IV inhibitors) and modulation of cytokine levels, as well as newer approaches to immunomodulation.

L27 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:450525 HCAPLUS
DOCUMENT NUMBER: 125:131396
TITLE: Phosphodiesterase type IV inhibitors
AUTHOR(S): Palfreyman, Malcolm N.; Souness, John E.
CORPORATE SOURCE: Rhone-Poulenc Rorer Central Research, Dagenham Research Centre, Dagenham, RM10 7XS, UK
SOURCE: Progress in Medicinal Chemistry (1996), 33, 1-52
CODEN: PMDCAY; ISSN: 0079-6468
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 306 refs.

L27 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN

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ACCESSION NUMBER: 1996:90747 HCAPLUS
DOCUMENT NUMBER: 124:193059
TITLE: Phosphodiesterase-IV inhibitors: novel therapeutics for the treatment of inflammatory diseases
AUTHOR(S): Lombardo, Louis J.
CORPORATE SOURCE: Wyeth-Ayers Res. Inc., Princeton, NJ, 08543-8000, USA
SOURCE: Current Pharmaceutical Design (1995), 1(2), 255-68
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 120 refs. The identification and characterization of the multiple isoforms of the phosphodiesterase enzyme has generated considerable interest in the preparation of selective inhibitors of these isoenzymes. Phosphodiesterase-IV (PDE-IV) is a cAMP-specific phosphodiesterase which has been shown to play an important role in the regulation of inflammatory and immune cell activation. Thus, it has been proposed that selective PDE-IV inhibitors may be useful for the treatment of inflammatory diseases. A diversity of structural types have been reported as selective PDE-IV inhibitors. Mol. modeling studies have played an important role in the discovery of these agents. An anal. of the structure-activity relationships (SAR) of novel inhibitors and their associated in vitro and in vivo profiles will be discussed.

L27 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:647285 HCAPLUS
DOCUMENT NUMBER: 123:73972
TITLE: Phosphodiesterase IV inhibitors: structural diversity and therapeutic potential in asthma
AUTHOR(S): Cavalla, David; Frith, Richard
CORPORATE SOURCE: Medicinal Chemistry, Napp Research Centre, Cambridge, CB4 4GW, UK
SOURCE: Current Medicinal Chemistry (1995), 2(1), 561-72
CODEN: CMCHE7; ISSN: 0929-8673
PUBLISHER: Bentham Science Publishers BV
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 127 refs. The phosphodiesterases (PDEs) represent a group of enzymes controlling levels of intracellular cAMP. Because of the ubiquitous effects of this intracellular messenger, inhibitors of these enzymes have widespread effects. Phosphodiesterase IV represents one of the five main families of PDE with a presence in smooth muscle and inflammatory cells, selective inhibition of which have been predicted to be of therapeutic advantage in asthma. There are 3 main classes of PDE IV inhibitor, relating to analogs of rolipram, nitraquazone, and xanthines. In vitro, PDE IV inhibitors are able to relax smooth muscle from the lung, and to reduce the production of inflammatory mediators from eosinophils, neutrophils, macrophages and lymphocytes. In vivo, these properties lead to bronchodilatation and inhibition of the late reaction and its sequelae that follow antigen challenge in sensitized animals. Clin. results to parallel these indicators of potential benefit in asthmatic patients have not yet been reported, but the panoply of potent and selective PDE IV inhibitors currently being progressed into the clinic will soon test this hypothesis.

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Updated Search

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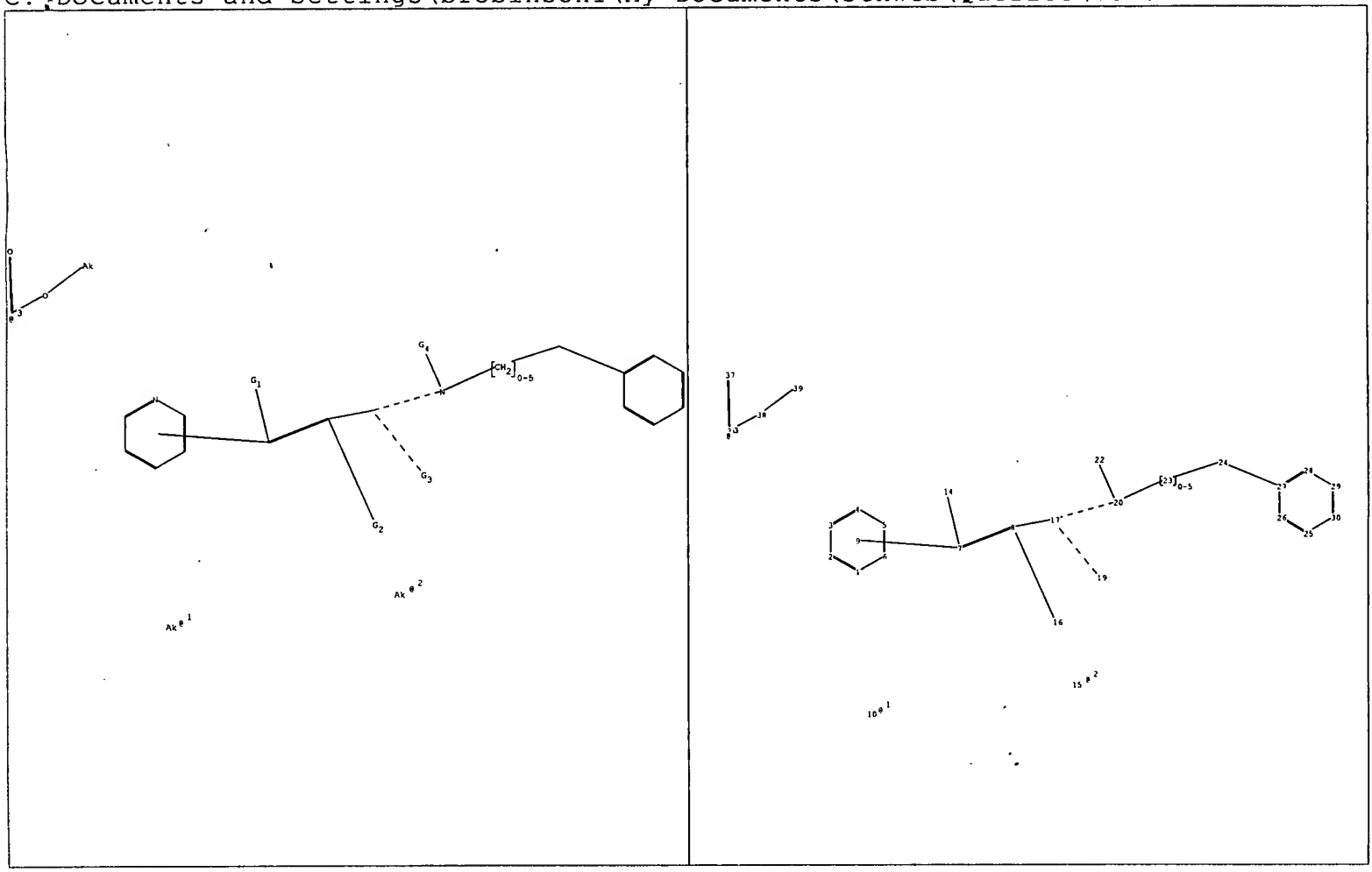

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ring nodes :
1 2 3 4 5 6 25 26 27 28 29 30
chain bonds :
7-8 7-14 8-16 8-17 17-19 17-20 20-22 20-23 23-24 24-27 36-37
36-38 38-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 25-26 25-30 26-27 27-28 28-29 29-30
exact/norm bonds :
7-14 8-16 17-19 17-20 20-22 36-37 36-38 38-39
exact bonds :
7-8 8-17 20-23 23-24 24-27
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 25-26 25-30 26-27 27-28 28-29 29-30
isolated ring systems :
containing 1 : 25 :

G1:H,Cb,[*1]

G3:O,S

G4:H,Ak

G5:H,CN,[*2],[*3]

Connectivity :
10:1 E exact RC ring/chain 15:1 E exact RC ring/chain
39:1 E exact RC ring/chain
Match level :
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10:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 19:CLASS 20:CLASS
22:CLASS 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom
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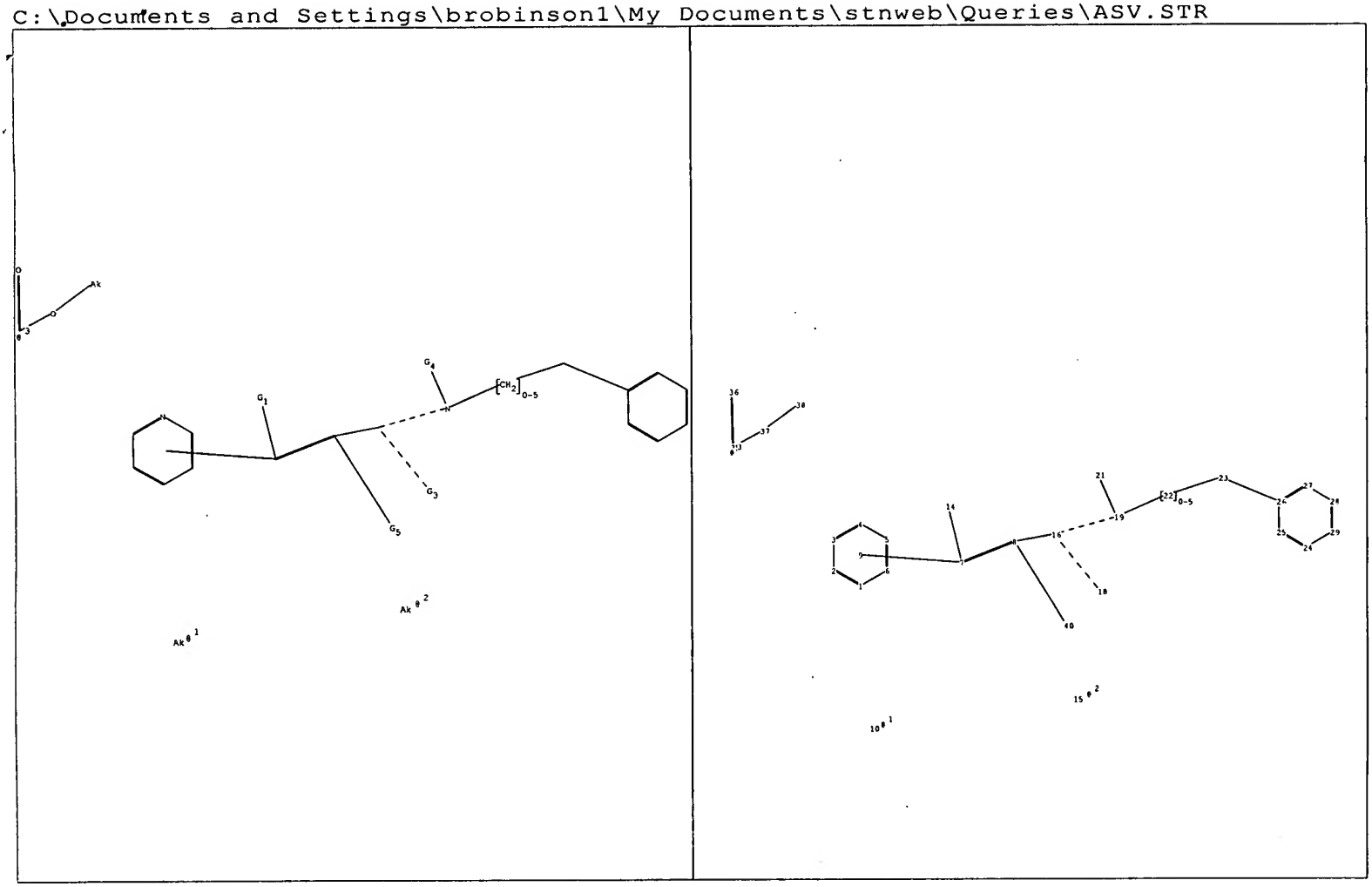

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7 8 10 14 15 16 18 19 21 22 23 35 36 37 38 40
ring nodes :
1 2 3 4 5 6 24 25 26 27 28 29
chain bonds :
7-8 7-14 8-16 8-40 16-18 16-19 19-21 19-22 22-23 23-26 35-36
35-37 37-38
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 24-25 24-29 25-26 26-27 27-28 28-29
exact/norm bonds :
7-14 8-40 16-18 16-19 19-21 35-36 35-37 37-38
exact bonds :
7-8 8-16 19-22 22-23 23-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 24-25 24-29 25-26 26-27 27-28 28-29
isolated ring systems :
containing 1 : 24 :

G1:H,Cb,[*1]

G3:O,S

G4:H,Ak

G5:H,CN,[*2],[*3]

Connectivity :
10:1 E exact RC ring/chain 15:1 E exact RC ring/chain
38:1 E exact RC ring/chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom
10:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 21:CLASS
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35:CLASS

36:CLASS 37:CLASS 38:CLASS 40:CLASS

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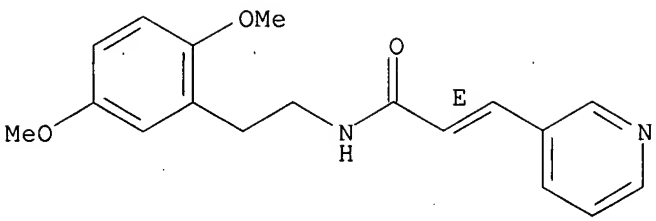
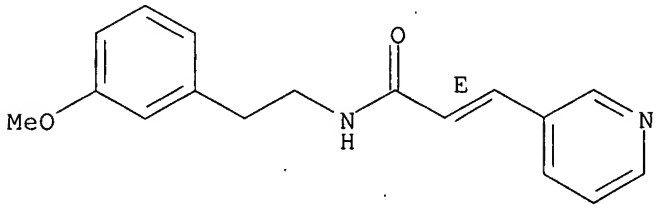


● HCl

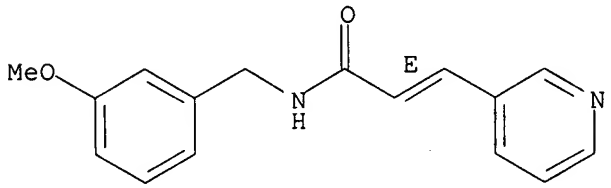
RN 637773-61-6 HCAPLUS
CN 2-Propenamide, N-[2-(3-methoxyphenyl)ethyl]-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



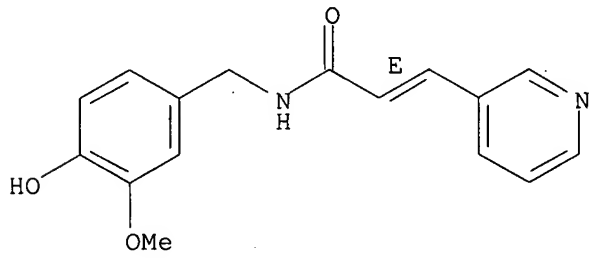
RN 637773-62-7 HCAPLUS
CN 2-Propenamide, N-[(3-methoxyphenyl)methyl]-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



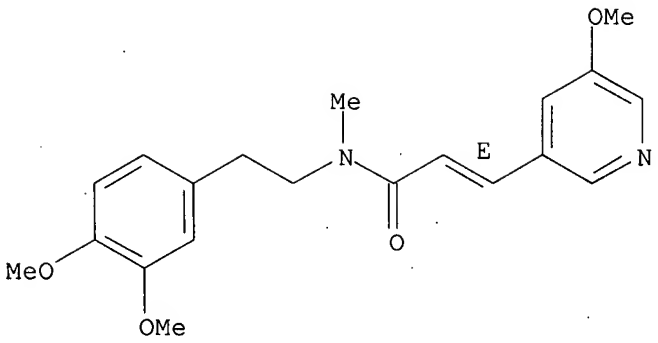
RN 637773-63-8 HCAPLUS
CN 2-Propenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



Updated Search

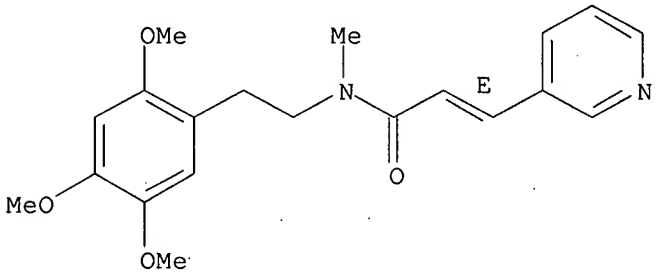
10510053



● HCl

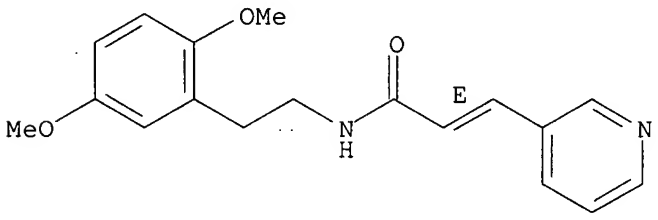
RN 637773-56-9 HCAPLUS
CN 2-Propenamide, N-methyl-3-(3-pyridinyl)-N-[2-(2,4,5-trimethoxyphenyl)ethyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-59-2 HCAPLUS
CN 2-Propenamide, N-[2-(2,5-dimethoxyphenyl)ethyl]-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

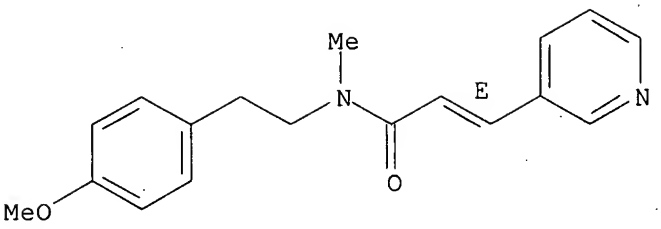
Double bond geometry as shown.



RN 637773-60-5 HCAPLUS
CN 2-Propenamide, N-[2-(2,5-dimethoxyphenyl)ethyl]-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

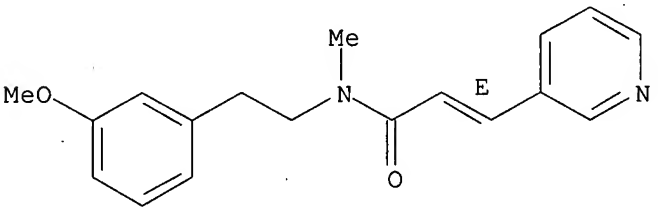
Double bond geometry as shown.

Updated Search



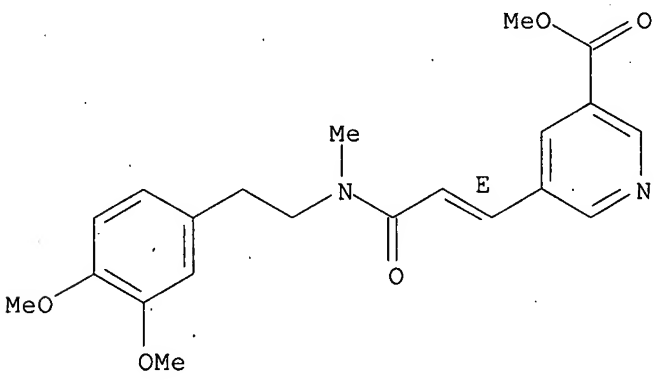
RN 637773-53-6 HCAPLUS
CN 2-Propenamide, N-[2-(3-methoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-54-7 HCAPLUS
CN 3-Pyridinecarboxylic acid, 5-[(1E)-3-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]-3-oxo-1-propenyl]-, methyl ester (9CI) (CA INDEX NAME)

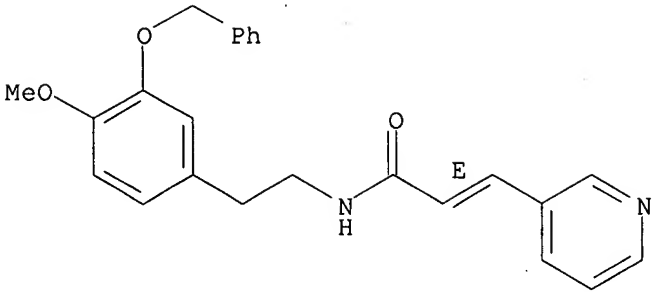
Double bond geometry as shown.



RN 637773-55-8 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-3-(5-methoxy-3-pyridinyl)-N-methyl-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

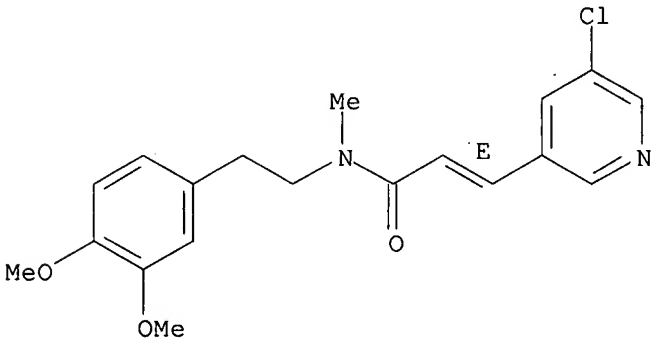
Double bond geometry as shown.

Updated Search



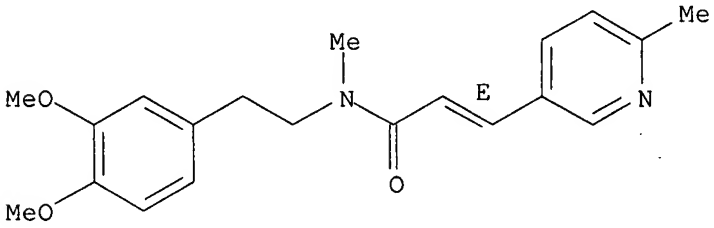
RN 637773-50-3 HCAPLUS
CN 2-Propenamide, 3-(5-chloro-3-pyridinyl)-N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-51-4 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(6-methyl-3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

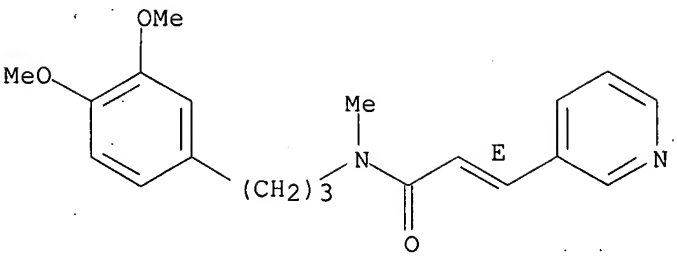
Double bond geometry as shown.



RN 637773-52-5 HCAPLUS
CN 2-Propenamide, N-[2-(4-methoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

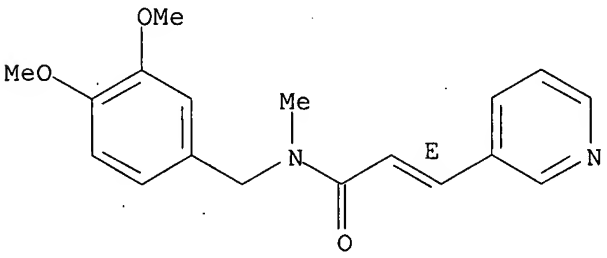
Double bond geometry as shown.

Updated Search



RN 637773-47-8 HCAPLUS
CN 2-Propenamide, N-[(3,4-dimethoxyphenyl)methyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

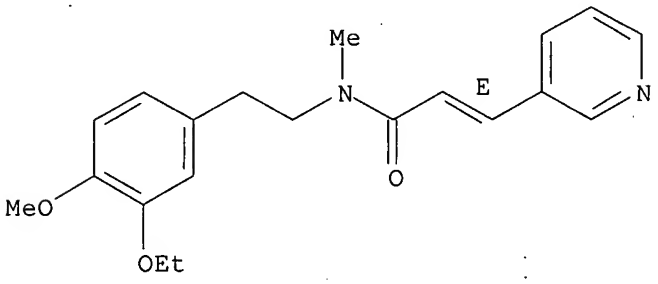
Double bond geometry as shown.



● HCl

RN 637773-48-9 HCAPLUS
CN 2-Propenamide, N-[2-(3-ethoxy-4-methoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



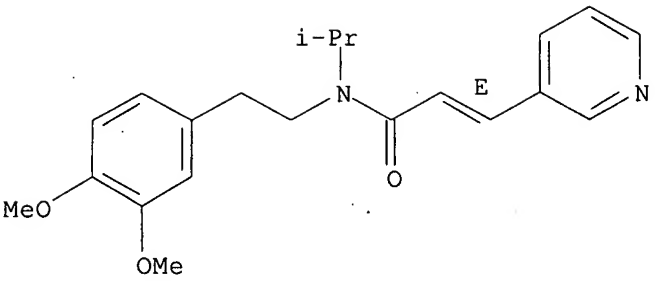
● HCl

RN 637773-49-0 HCAPLUS
CN 2-Propenamide, N-[2-[4-methoxy-3-(phenylmethoxy)phenyl]ethyl]-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

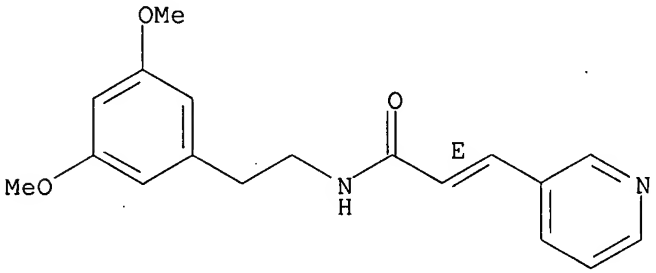
Updated Search

10510053



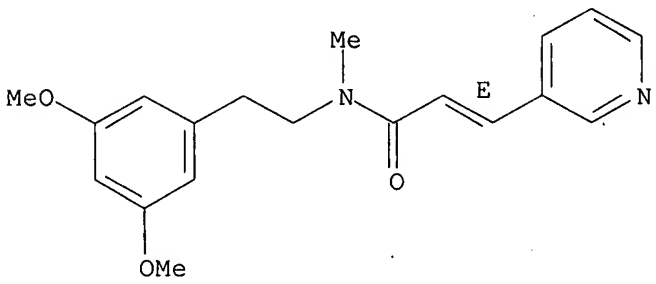
RN 637773-44-5 HCAPLUS
CN 2-Propenamide, N-[2-(3,5-dimethoxyphenyl)ethyl]-3-(3-pyridinyl)-, (2E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-45-6 HCAPLUS
CN 2-Propenamide, N-[2-(3,5-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

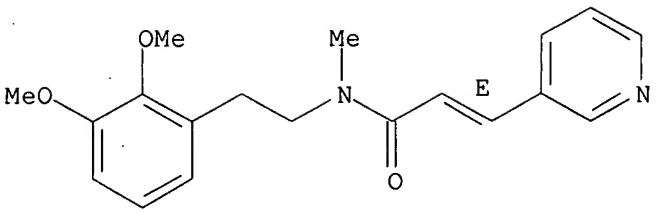
Double bond geometry as shown.



RN 637773-46-7 HCAPLUS
CN 2-Propenamide, N-[3-(3,4-dimethoxyphenyl)propyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

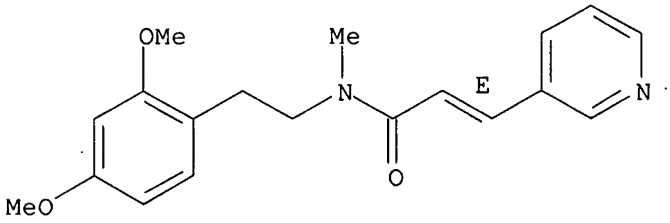
Updated Search



● HCl

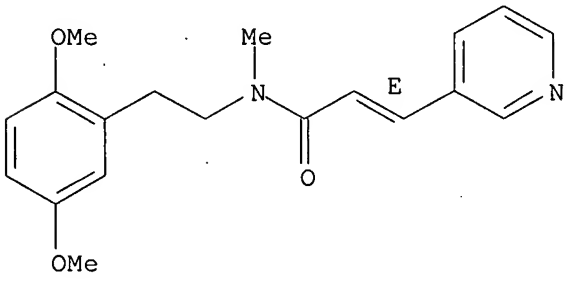
RN 637773-41-2 HCAPLUS
CN 2-Propenamide, N-[2-(2,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-42-3 HCAPLUS
CN 2-Propenamide, N-[2-(2,5-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

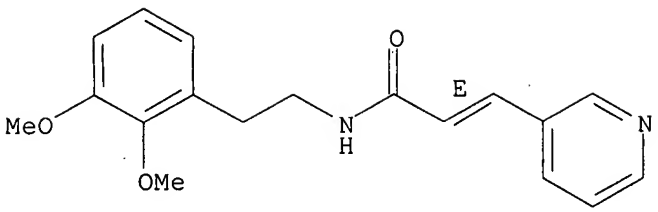


● HCl

RN 637773-43-4 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-(1-methylethyl)-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

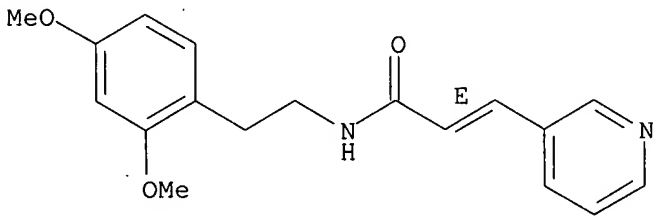
Updated Search



● HCl

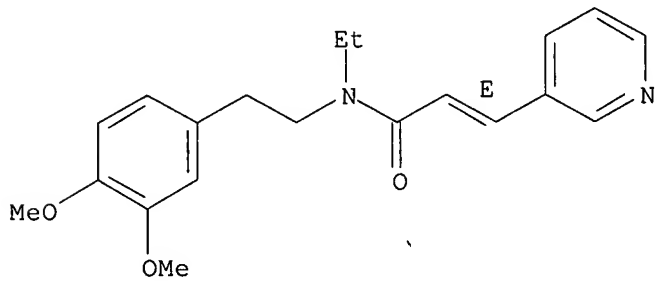
RN 637773-38-7 HCAPLUS
CN 2-Propenamide, N-[2-(2,4-dimethoxyphenyl)ethyl]-3-(3-pyridinyl)-, (2E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-39-8 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-ethyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



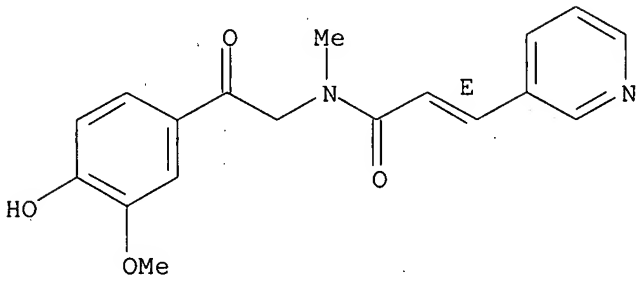
RN 637773-40-1 HCAPLUS
CN 2-Propenamide, N-[2-(2,3-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

Updated Search

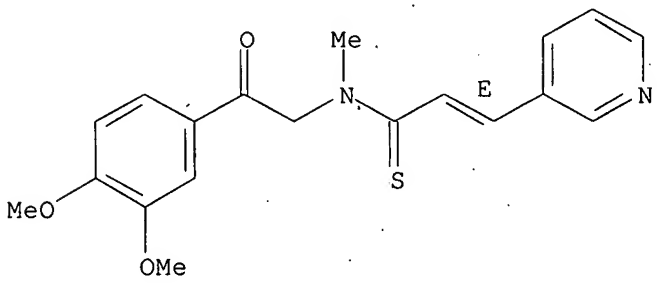
pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

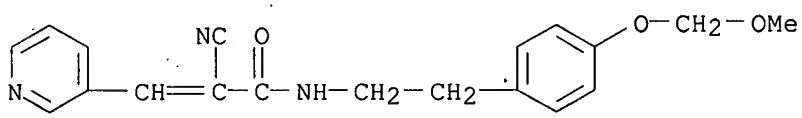


RN 219965-76-1 HCAPLUS
CN 2-Propenethioamide, N-[2-(3,4-dimethoxyphenyl)-2-oxoethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-36-5 HCAPLUS
CN 2-Propenamide, 2-cyano-N-[2-[4-(methoxymethoxy)phenyl]ethyl]-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)

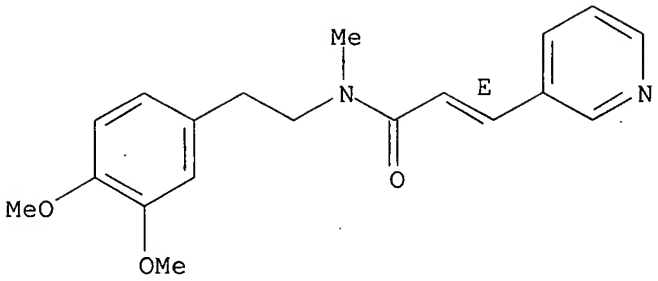


RN 637773-37-6 HCAPLUS
CN 2-Propenamide, N-[2-(2,3-dimethoxyphenyl)ethyl]-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

Updated Search

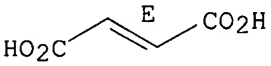
10510053



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

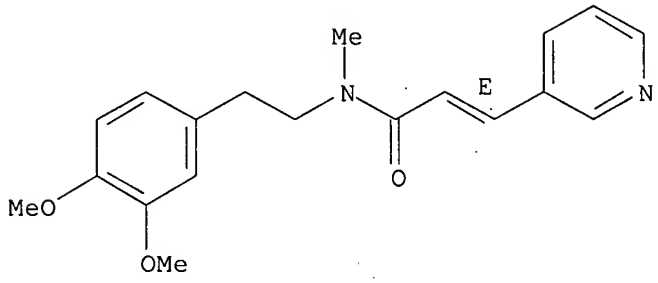


RN 219965-58-9 HCAPLUS
CN Butanedioic acid, compd. with (2E)-N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-2-propenamide (1:1) (9CI) (CA INDEX NAME)

CM 1

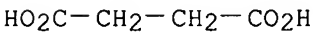
CRN 219964-53-1
CMF C19 H22 N2 O3

Double bond geometry as shown.



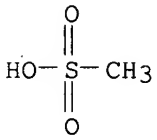
CM 2

CRN 110-15-6
CMF C4 H6 O4



RN 219965-73-8 HCAPLUS
CN 2-Propenamide, N-[2-(4-hydroxy-3-methoxyphenyl)-2-oxoethyl]-N-methyl-3-(3-

Updated Search

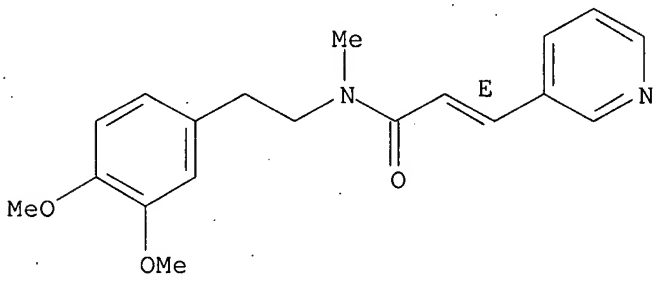


RN 219965-56-7 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

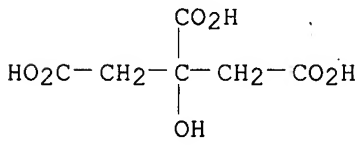
CRN 219964-53-1
CMF C19 H22 N2 O3

Double bond geometry as shown.



CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 219965-57-8 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 219964-53-1
CMF C19 H22 N2 O3

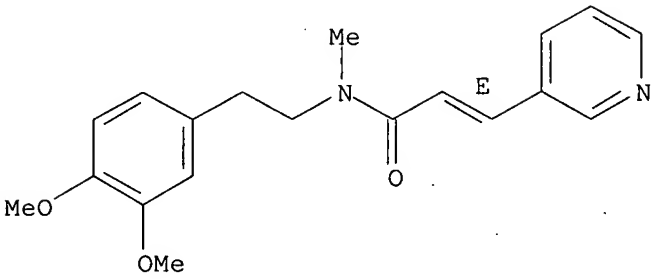
Double bond geometry as shown.

Updated Search

10510053

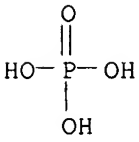
CRN 219964-53-1
CMF C19 H22 N2 O3

Double bond geometry as shown.



CM 2

CRN 7664-38-2
CMF H3 O4 P

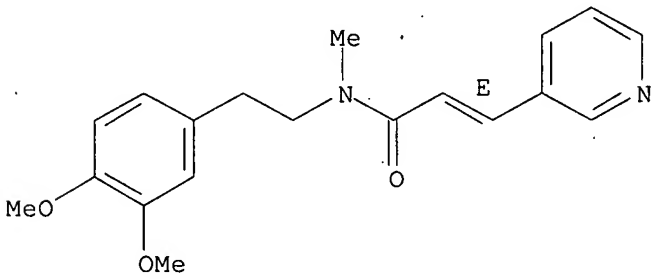


RN 219965-55-6 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 219964-53-1
CMF C19 H22 N2 O3

Double bond geometry as shown.

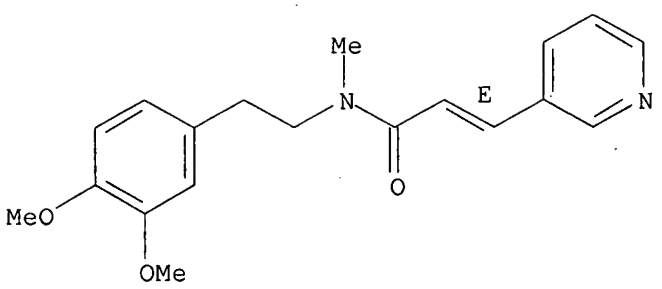


CM 2

CRN 75-75-2
CMF C H4 O3 S

Updated Search

10510053



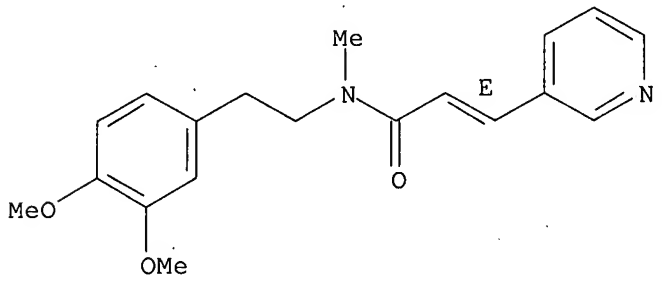
● HBr

RN 219965-53-4 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

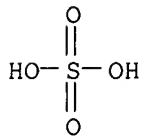
CRN 219964-53-1
CMF C19 H22 N2 O3

Double bond geometry as shown.



CM 2

CRN 7664-93-9
CMF H2 O4 S



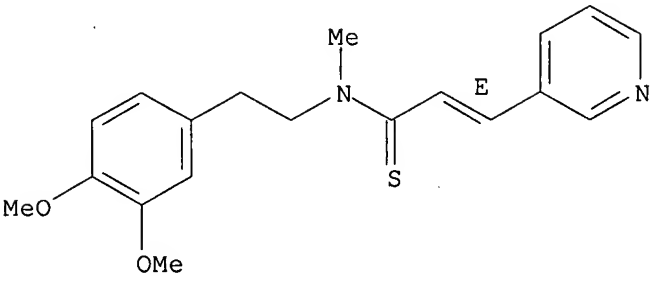
RN 219965-54-5 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

Updated Search

10510053

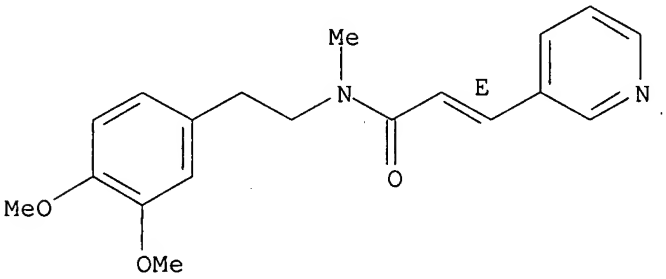
Double bond geometry as shown.



● HCl

RN 219965-51-2 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HCl

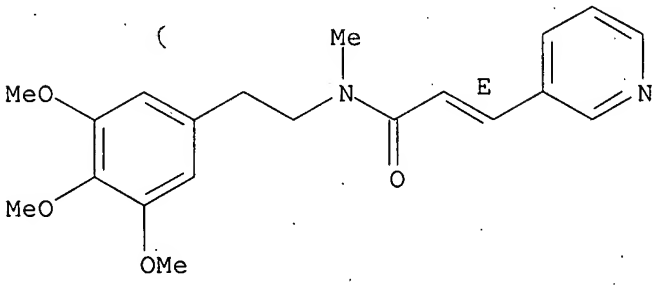
RN 219965-52-3 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrobromide, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

Updated Search

trimethoxyphenyl)ethyl]-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

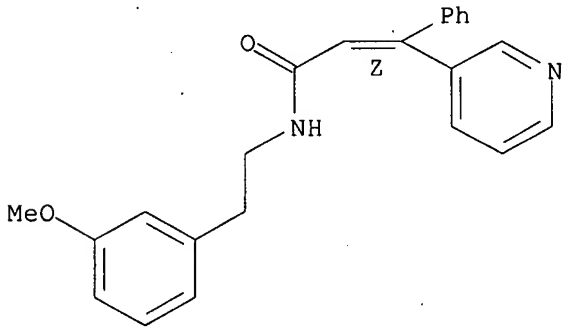
Double bond geometry as shown.



● HCl

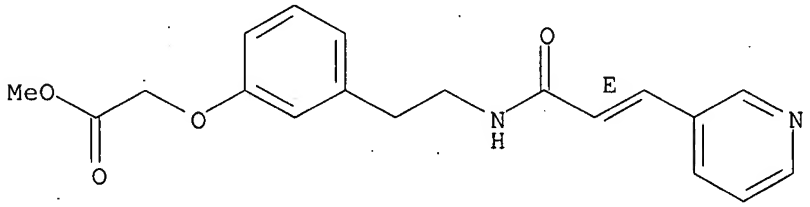
RN 219964-38-2 HCAPLUS
CN 2-Propenamide, N-[2-(3-methoxyphenyl)ethyl]-3-phenyl-3-(3-pyridinyl)-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 219964-68-8 HCAPLUS
CN Acetic acid, [3-[2-[[(2E)-1-oxo-3-(3-pyridinyl)-2-propenyl]amino]ethyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

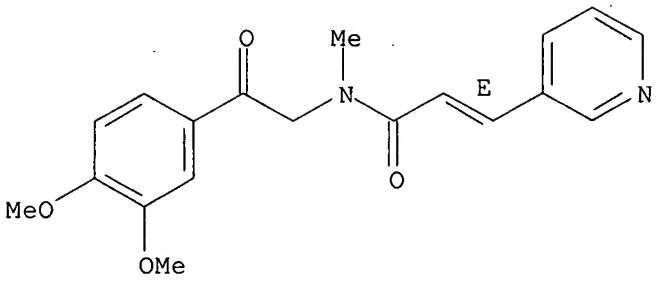
Double bond geometry as shown.



RN 219965-44-3 HCAPLUS
CN 2-Propenethioamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Updated Search

10510053



IT 219963-67-4P 219963-74-3P 219964-38-2P
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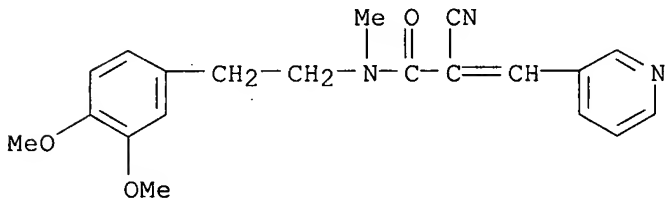
637773-97-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyridylacrylamides as phosphodiesterase IV inhibitors)

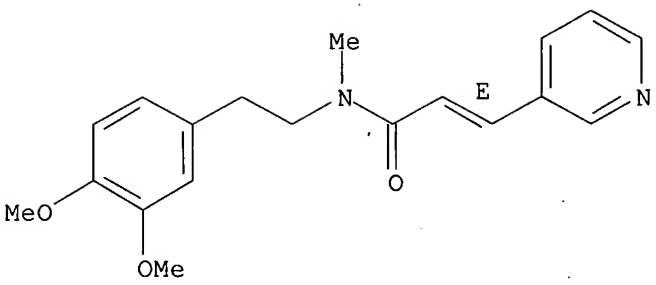
RN 219963-67-4 HCAPLUS
CN 2-Propenamide, 2-cyano-N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

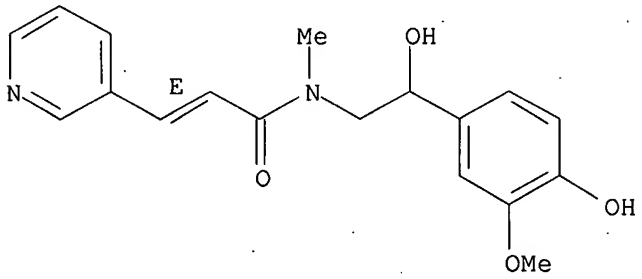
RN 219963-74-3 HCAPLUS
CN 2-Propenamide, N-methyl-3-(3-pyridinyl)-N-[2-(3,4,5-

Updated Search



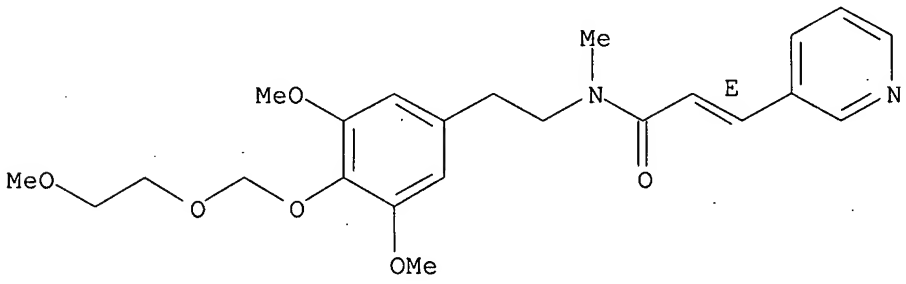
RN 219965-69-2 HCAPLUS
CN 2-Propenamide, N-[2-hydroxy-2-(4-hydroxy-3-methoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-57-0 HCAPLUS
CN 2-Propenamide, N-[2-[3,5-dimethoxy-4-[(2-methoxyethoxy)methoxy]phenyl]ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 637773-88-7 HCAPLUS
CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)-2-oxoethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

Updated Search

	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003236340		A1	20031027	AU 2003-236340	20030402
BR 2003008935		A	20050104	BR 2003-8935	20030402
EP 1495757		A1	20050112	EP 2003-746165	20030402
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
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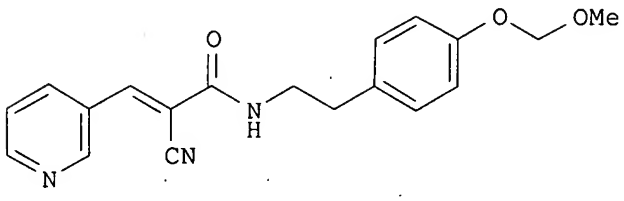
US 2005187264		A1	20050825	US 2005-510053	20050412
PRIORITY APPLN. INFO.:				JP 2002-99491 A	20020402
				WO 2003-JP4227 W	20030402

OTHER SOURCE(S): MARPAT 140:59516

GI



I

AB The title compds. with general formula of Ar1-C(R1)=C(R2)-C(=X)-N(R3)-(CH2)n-1-C(A)(B)-Ar2 [wherein Ar1 = (un)substituted Py; Ar2 = substituted Ph; R1 = H, alkyl, or aryl; R2 = H, alkyl, CN, or alkoxycarbonyl; R3 = H or (un)substituted alkyl; X = O or S; A and B = independently H, OH, alkoxy, or alkylthio; or A and B together form oxo, thioxo, or (un)substituted imino, etc.; n = 1-3] or pharmaceutically acceptable salts thereof are prepared as phosphodiesterase IV inhibitors. For example, 4-(methoxymethoxy)phenethylamine was reacted with cyanoacetic acid in DMF in the presence of diethylphosphoryl cyanide and Et3N to give 2-cyano-N-(4-methoxymethoxyphenethyl)acetamide (45%). The acetamide obtained was treated with 3-pyridinecarboxaldehyde in ethanol in the presence of a little amount of piperidine to afford I (64%). The title compds. showed inhibitory activity of 43 to 86 μM against human phosphodiesterase IV.

IT 219964-53-1P 219965-69-2P 637773-57-0P
637773-88-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of pyridylacrylamides as phosphodiesterase IV inhibitors)

RN 219964-53-1 HCAPLUS

CN 2-Propenamide, N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methyl-3-(3-pyridinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

10510053

FILE 'HCAPLUS' ENTERED AT 19:33:52 ON 11 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 11 Sep 2007 VOL 147 ISS 12
FILE LAST UPDATED: 10 Sep 2007 (20070910/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> S L17
L18 42 L17

=> S L18 AND HATTORI, T?/AU
4613 HATTORI, T?/AU
L19 2 L18 AND HATTORI, T?/AU

=> D L19, IBIB ABS HITSTR, 1-2

L19 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:836850 HCAPLUS
DOCUMENT NUMBER: 140:59516
TITLE: Preparation of pyridylacrylamides as phosphodiesterase IV inhibitors
INVENTOR(S): Hattori, Tomohisa; Sasaki, Toshinobu; Hasegawa, Yoshihiro; Obata, Tatsuhiro
PATENT ASSIGNEE(S): Tsumura & Co., Japan
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086396	A1	20031023	WO 2003-JP4227	20030402
WO 2003086396	A9	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

Updated Search

10510053

L14 STRUCTURE UPLOADED

=> D L14
L14 HAS NO ANSWERS
L14 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> S L14
SEARCH FAILED DUE TO A STRUCTURE QUERY ERROR
The structure query could not be searched. Please review and revise your structure query, especially checking the variable definitions and attachments. In rare instances the failure may be due to a system problem. Please contact your local STN Help Desk if you need assistance.

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L15 STRUCTURE UPLOADED

=> S L15
SAMPLE SEARCH INITIATED 19:33:44 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1068 TO ITERATE

100.0% PROCESSED 1068 ITERATIONS 22 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 19400 TO 23320
PROJECTED ANSWERS: 159 TO 721

L16 22 SEA SSS SAM L15

=> S L15 FULL
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 171.65 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:Y
FULL SEARCH INITIATED 19:33:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 20969 TO ITERATE

100.0% PROCESSED 20969 ITERATIONS 484 ANSWERS
SEARCH TIME: 00.00.01

L17 484 SEA SSS FUL L15

=> FILE HCAPLUS

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.55	456.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-14.04

Updated Search